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Abstract Title:- Effect of Andrographolide on p21 and HER2 signalling in Colorectal Cancer cell lines

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Aims:-Colon Cancer, also known as Colorectal Cancer (CRC), is the second most common form of malignancy that results in fatalities worldwide. Human Epidermal Growth Factor Receptor 2 (HER2) is known to be overexpressed in some CRC patients and is also established as a known prognostic marker. It is also known to be associated with the development of resistance that is often seen during cancer treatment due to its increased trafficking and recycling. In normal cells, p21 is a well-known checkpoint for cell cycle and acts in an antiproliferative manner but its expression is influenced and dysregulated by the onset of cancer.

In order to overcome the problems seen during the onset of disease and treatment, wide varieties of plant products have been tested which can modify the effect of HER2 and p21 signalling mechanisms. Andrographolide is one such plant product which has been shown to have influenced the onset, progression, and treatment of cancer. Based on the previous literature it was hypothesised that Andrographolide induces apoptosis in cancer cell lines by lowering HER2 expression as well its recycling and by affecting p21 levels. To prove this hypothesis, experiments were performed in vitro using HCT 116 and HT 29 cell lines.

Methods:- Cell lines HCT 116 and HT 29 were procured from NCCS (Pune), India and grown in RPMI 1640 media supplemented with 10% FBS. MTT assay was done to determine the IC50 of Andrographolide in both the cell lines. The statistical analysis for IC50 value was done using GraphPad Prism 10 after 24 hours of treatment. Batches of cells were then treated using 0-80 µM Andrographolide. To determine mRNA expression of p21 and HER2 in these treated cells, q-RT-PCR was done. To further verify the protein levels, Western Blotting for the two target proteins HER2 and p21 was done using cell lysates. Additionally, to check the degradation of HER2 using Lysotracker Dye as well as localisation of p21, cells were grown on cover slips, treated with the drug in the same range as before, and subjected to immunofluorescence.

Results:- The results showed decreased levels of HER2 due to increased degradation of the protein. The p21 levels were also found to be dysregulated.

Conclusions:- Overall, the results suggest that Andrographolide inhibits cell proliferation and can be used as an adjuvant in combinatorial therapies.

Keywords:- Colorectal Cancer, HER2, p21, Andrographolide, in vitro study